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Malignant Lymphoma of Thyroid Associated with Chronic Lymphocytic Thyroiditis and Occult Sclerosing Carcinoma

—A case report—

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Although the reported number of malignant lymphoma of the thyroid has been increased[1~5], primary malignant lymphoma of the thyroid associated with chronic lymphocytic thyroiditis has been sporadically reported since its first description by Graham in 1931. The apparent coexistence of these two conditions has undoubtedly been noted by other observers[6~12]. And they suggested that malignant lymphoma of the thyroid might arise from the lymphoid tissue in a wide variety of preexisting thyroidal disease. This report was made to record a case of primary thyroid lymphoma recently seen in this department with special emphasis on the associated thyroiditic changes in the uninvolved portion of the gland, which suggest the antecedent presence of chronic lymphocytic thyroiditis.

CASE REPORT

This patient was a 60-year-old woman who noted a mass in the anterior neck two months prior to her initial medical examination. This finding was followed by a gradual enlargement of her right thyroid lobe and subsequent mild enlargement of the left with pressure symptoms, principally dyspnea and vague esophageal discomfort. The patient had a past history of uncontrolled hypertention and diabetes mellitus without specific treatment for previous two years. Physical examination revealed a nodular enlargement of the right thyroid gland which was hard, fixed and nontender. Several lymph nodes were palpable in the right supraclavicular area without clinical evidence of metastasis to other sites of the body. Thyroid function tests were all within normal limits except for increased antimicrosomal antibody and antithyroglobulin antibody in her serum. X-ray film taken at the time of admission demonstrated displacement of tracheal air colum to the left. Thyroid scan showed a large space occupying lesion in the right thyroid and, was interpreted as a malignant tumor of the thyroid. Total thyroidectomy was performed. Operation findings were well conformed to malignant tumor. Extrathyroidal soft tissue as well as trachea and esophagus were all involved by the neoplastic and fibrotic process. A small isolated nodule was also seen in contralateral thyroid lobe. Grossly, the gland was diffusely enlarged, coarsely lobated and mea-

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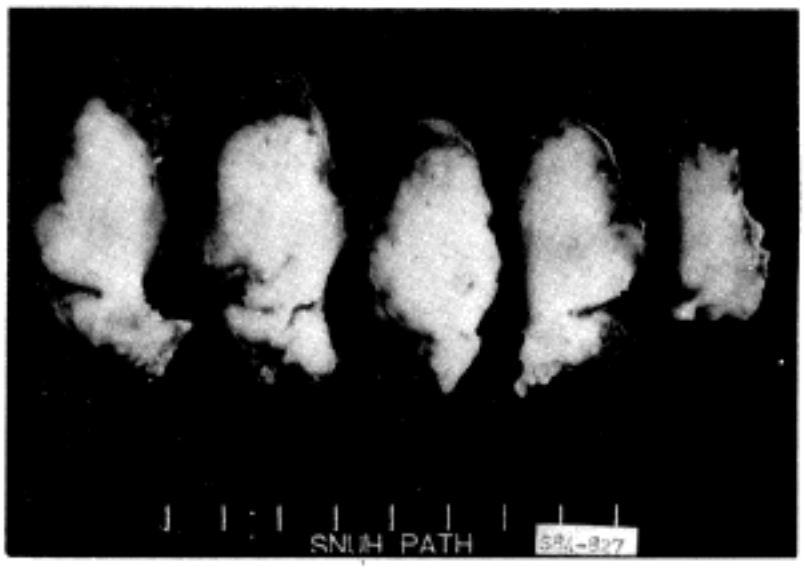

Fig. 1. Cut surface of thyroid showing lobulated and homogeneous mass with compressed rim of thyroid tissue

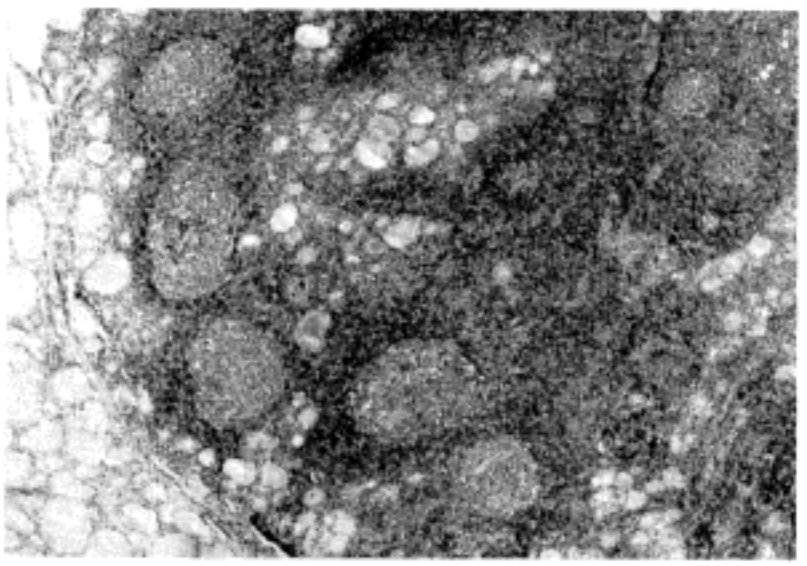

Fig. 3. Areas of chronic lymphcytic thyroiditis with prominent germinal centers. (H&E, ×40)

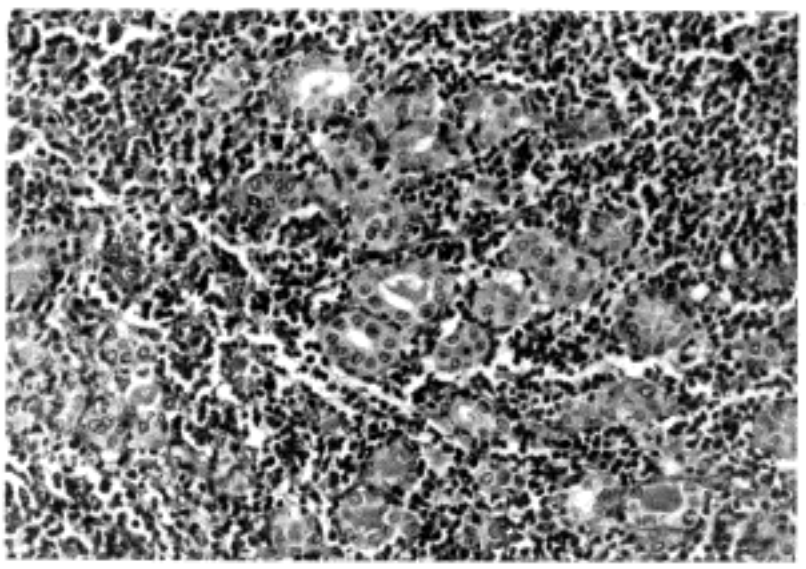

Fig. 2. Residual thyroid follicles with oxyphilic or ballooning change surrounded by diffuse lymphocytic infiltration (H&E, ×200)

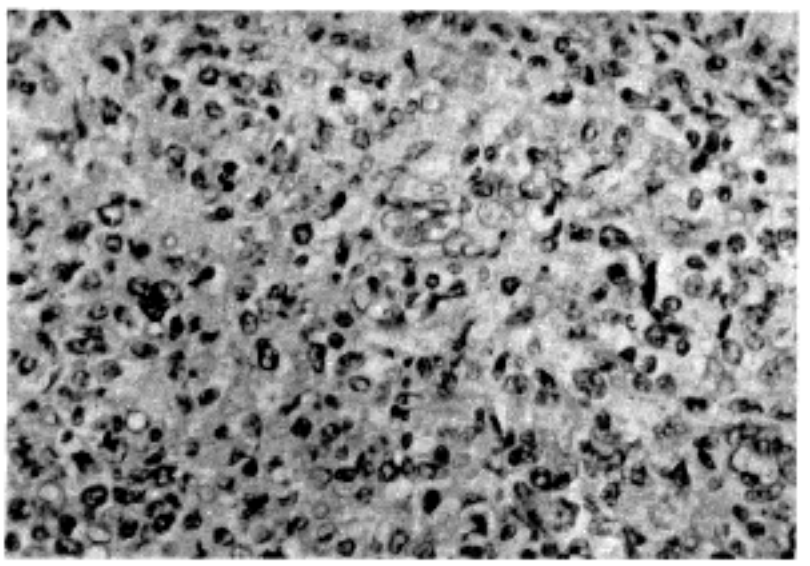

Fig. 4. The mass composed of mixture of neoplastic small and large lymphcytes. (H&E, ×400)

sured 6×8×2.5 cm. The cut surface was homogeneously grayish white with peripheral narrow rim of normal appearing thyroid parenchyme. Distinct capsulation was not seen (Fig. 1).

Microscopically, the non-neoplastic area was composed of atrophic and partially oxyphilic thyroid follicles with condensed colloid content and activated secondary lymphoid follicles (Fig. 2). Lymphoid follicles were irregular in shape and size, and some of which were apparently intermingled with obviously neoplastic area, partly demonstrating nodular pattern of malignancy (Fig. 3). In the largest portion of the mass, epithelium was absent and the tissue was replaced completely by mixture of neoplastic small and large lymphocytes (Fig. 4). Areas were seen that showed neoplastic lymphoid cells infiltrating entire thickness of the walls of blood vessels within the thyroid parenchyme and adjacent extrathyroid tissue, including fibroadipose tissue and skeletal muscle. There was a focus of occult sclerosing carcinoma, which was papillary type and measured 0.3 cm in maximum diameter in the non-neoplastic area (Fig. 5). A diagnosis of malignant lymphoma, diffuse mixed lymphocytic and histiocytic type asso-

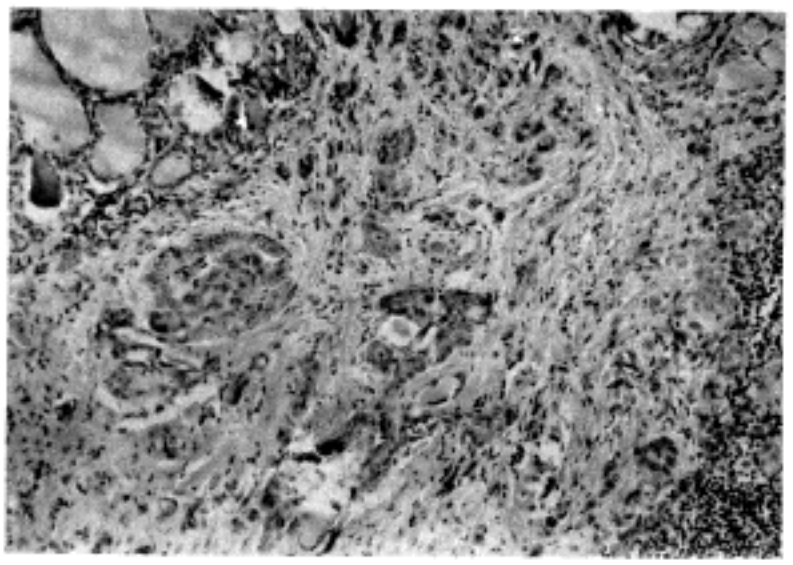

Fig. 5. One focus of occult sclerosing carcinoma within the non-neoplastic portion of thyroid. (H&E, ×100)

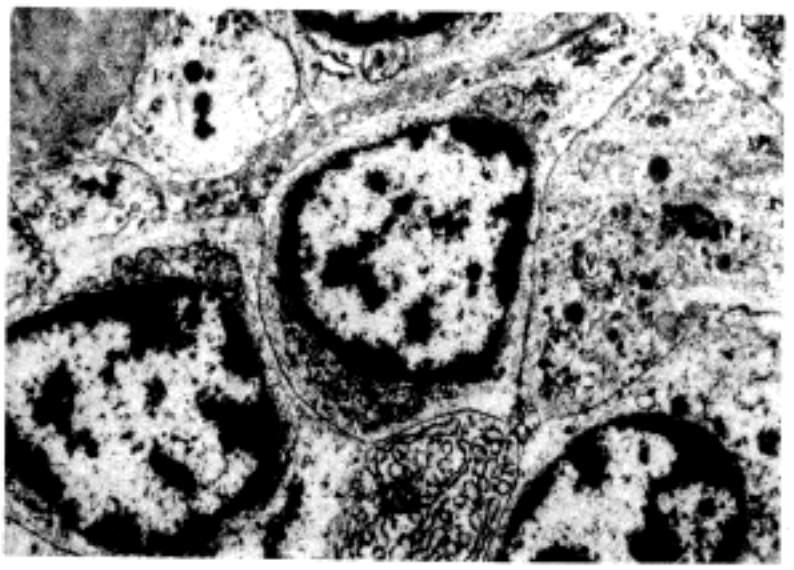

Fig. 6. Ultrastructural features of tumor cells showing paucity of cytoplasmic organelles and absence of tight junction and neurosecretory granules (×14,000)

ciated with chronic lymphocytic thyroiditis and occult sclerosing carcinoma was made on the basis of the findings described above.

Ultrastructural examination of tumor cells confirmed that the malignant cells were lymphocytes, probably transformed follicular center cells. The nuclei were generally round, occasionally indented and had finely dispersed heterochromatin. There was a paucity of cytoplasmic organelles except for dilated cisternae of endoplasmic reticulum and a few mitochondria. Characteristic features of epithelial cells and parafollicular c-cells, such as tight junctions, hemidesmosomal connections and neurosecretory granules were not present (Fig. 6).

PAP(peroxidase antiperoxidase complex), using antihuman immunogloblin G.M.A. and light chain κ. and λ, was performed in neoplastic and non-neoplastic portions of this lesion. Occasional κ positive cells were demonstrated in the tumor portion which is contrast to polyclonal positivity in thyroiditic areas. This immunohistochemical results strongly suggest, though not definite, origin of this lymphoma from B lymphocytes.

DISCUSSION

The histologic association between primary malignant lymphoma of the thyroid and chronic lymphocytic thyroiditis might indicate a causal relationship between chronic antigenically stimulated tissue and the development of lymphoma, thus suggesting the possible origination of lymphoma from transformed lymphocytes. In 1977, Burke and Butler presented the definite association of primary malignant lymphoma of the thyroid with chronic lymphocytic thyroiditis in 27 of the 35 cases[12]. They stated that the type of thyroiditis ranged from mild and focal chronic lymphocytic thyroiditis to typical Hashimoto thyroiditis with Hürthle cell change of thyrocytes. The neoplastic portions were histiocytic lymphomas with only one exception which was poorly differentiated lymphocytic type. They also observed an apparent subtle transition of the hyperplastic type of chronic thyroiditis to a nodular type of malignant lymphoma. In our case, the portion of the thyroid not involved by neoplasm showed the variable sized follicles formed by ballooned and oxyphilic thy-

rocytes. These follicles were arranged in clumps and were surrounded by broad zones of lymphocytes, partly forming activated lymphoid follicles. These changes were diffuse throughout the non-neoplastic thyroid parenchyme and were consistent with a diagnosis of chronic lymphocytic thyroiditis. The pattern of malignant lymphoma was well evidenced by the infiltration of neoplastic lymphoid cells, total parenchymal effacement and homogeneous population of follicular center cells. The tumor was confined with the thyroid gland and showed no other clinically demonstrable focus of tumor. Demonstration of increased autoantibody, such as antimicrosomal and antithyroglobulin antibodies in this case would be an additional supportive data for definite presence of the immune-mediated chronic lymphocytic thyroiditis. Subtle transitional zone between chronic lymphocytic thyroiditis and diffuse lymphoma was present with vague nodular configuration. All these pathologic findings were quite similar to those of Burke's series. Electron microscopic study of these neoplastic cells, which was performed for differentiation from anaplastic carcinoma of small cell type or meudllary carcinoma revealed the features of transformed lymphocytes rather than those of parafollicular c-cell and epithelial cells. Occult sclerosing carcinoma of 3 mm-diameter was detected in non-neoplastic thyroid parenchyme. This lesion was considered to be mere incidental finding without any particular relationship to either malignant lymphoma or chronic lymphocytic thyroiditis[13,14].

SUMMARY

Authours have recently experienced a case of thyroid lymphoma associated chronic lymphocytic thyroiditis in a 60-year-old female. Examination of the marginal non-neoplastic thyroid tissue showed changes consistent with chronic lymphocytic thyroiditis with hyperactive lymphoid follicles. And this lesion was serologically proved by increased antimicrosomal and antithyroglobulin antibody titers. Transitional zones, mimicking nodular lymphoma between these two diseases also was present. The importance of these changes has been clearly understood by many authors, We suspected that it might serve in the clarification of histogenesis of primary thyroid lymphoma, namely secondary transformation from preexisting chronic lymphocytic thyroiditis. An occult sclerosing carcinoma found incidentally was considered to have no specific pathogenetic relationship with either lymphoma or chronic lymphocytic thyroiditis.

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=국문초록=

만성 림프구성 갑상선염을 동반한 갑상선의 악성 림프종

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서연림 · 박성희 · 김용일

갑상선에서 생기는 원발성 악성 림프종 및 다른 림프구 증식성 병변에 대한 보고가 최근 증가하고 있으며, 대부분의 저자들은 이 두병변이 거의 모든 예에서 공존한다고 보고했으며, 이들 두 병변의 공존은 악성 림프종의 발생과 밀접한 관계가 있다고 주장하였다. 즉 선행하고 있었던 만성 갑상선염에서 병리조직학적으로 관찰되는 림프구가 지속적인 항원의 자극을 받음으로써 종양성 림프구로 변환되어 종국에는 악성 림프종을 유발한다는 주장이다. 이것을 뒷받침해 주는 소견으로는 대부분의 환자의 혈청내에서 anti-thyroglobulin antibody와 antimicrosomal antibody가 검출되며, 종양의 전자현미경적 관찰에서도 종양을 구성하고 있는 세포의 미세구조가 변환된 림프구와 통일한 소견을 보이는 것이다.

최근 저자들은 60세된 여자의 외과적으로 적출된 갑상선에서 악성 림프종에 수반된 만성 림프구성 갑상선염과 유두상 미소 종양(occult sclerosing carcinoma)이 관찰되어, 이 병변의 광학현미경 및 전자현미경, PAP 염색등을 시행하고, 그 특징적인 병리조직학적 소견을 기술하였다.